DISSERTATION

on

Clinical Profile of Hypokalemic Periodic Paralysis

M.D., DEGREE EXAMINATION

BRANCH-I, GENERAL MEDICINE

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Chennai

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DECLARATION

I solemnly declare that this Dissertation entitled **"Clinical Profile of Hypokalemic Periodic Paralysis"** was done by me at Madras Medical College and Government General Hospital during 2004-2007 under the guidance and supervision of **Prof. K. RAGHAVAN.** This dissertation is submitted to the Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfillment of requirements for the award of **M.D., Degree in General Medicine, Branch-I.**

Place :

Date : **Dr. K. MAYILANANTHI**

CERTIFICATE

This is to certify that the Dissertation entitled **"Clinical Profile of Hypokalemic Periodic Paralysis "** is a bonafide work done by **Dr. K. MAYILANANTHI,** at Madras Medical College, Chennai in partial fulfillment of the University rules and regulations for award of **M.D., Degree in General Medicine** under my guidance and supervision during the academic period from May, 2004-2007.

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INTRODUCTION

Muscle weakness is associated with a number of different electrolyte disorders including hyperkalemia, hypercalcemia and hypo or hyper magnesemia.However, hypokalemia emerges as the most prevalent cause of periodic paralysis

Periodic paralysis includes a range of unique disorders and syndromes of varying genetic origin and symptomatology. The discovery of the adult human skeletal muscle voltage dependant channel had led to the discovery of specific gene lesions in different portion of the channel structure that are associated primarily with the potassium sensitive periodic paralysis.

Autosomal dominant mutations in the CACNAIS gene[4] encoding the α_1 subunit of L-type calcium channels are the most common genetic cause of hypokalemic periodic paralysis. Whereas type II hypokalemic periodic paralysis is caused by mutations in the SCN4A gene[2] encoding the skeletal sodium channel.

Clinical and laboratory investigations are in progress to determine the relationship between the phenotype and the genotype in families having different form of muscle diseases with known genetic defects affecting the skeletal muscle sodium channel.

The case study described in detail in the subsequent pages will give some knowledge about preventing acute attacks of hypokalemic periodic paralysis, diagnosing it at its onset and to treat it promptly, so that injury to the muscle can be limited and the patient saved.

This study will also give some information about myopathic forms, which usually presents with progressive muscle weakness without any history of episodic paralysis that can be diagnosed by muscle biopsy.

This will also highlight the importance of family history and past history of similar weakness as these patients and the family members who carry the mutations are at slightly increased risk of developing malignant hyperthermia in the peri-operative time.

REVIEW OF LITERATURE

HISTORICAL BACKGROUND:

Hypokalemic Periodic paralysis is the best known form of periodic paralysis. The history of this disease is difficult to trace, but the first unmistakable account was probably that of Hartwig in 1874, followed by the accounts of Westphal in 1885 and Oppenheim in 1891. Goldflam in 1895 first called attention to the remarkable vacuolization of the muscle fibers that is characteristic of the process.

In 1937, Aitken and associates described the occurrence of low serum potassium during attacks of paralysis and reversal of the paralysis by administration of potassium, thus setting the stage for subsequent differentiation of the hyperkalemic forms of periodic paralysis.

Talbott's monograph serves as the best historical review of the subject, and includes all cases that have been reported prior to 1941. The most recent reviews by Layzer and by Lehmann, Horn and Engel and their associates bring the subject largely up to date.

The disease has been observed in all parts of the world . Periodic paralysis can be broadly classified as two types.

1. Primary
2. Secondary

Primary Periodic Paralysis (also known as channelopathies)[20]

Here, the diagnosis is based on history and confirmed by appropriate evaluation of electrolytes.

It is classified as:

1. Hypokalemic periodic paralysis
2. Hyperkalemic periodic paralysis
3. Anderson's disease
4. Paramyotonia congenita

The differences between the various form of channelopathies are given in table-I.

Differential diagnosis for secondary hypokalemic periodic paralysis[6]

1. Thyrotoxic periodic paralysis
2. Periodic Paralysis secondary to renal potassium wastage
3. Periodic Paralysis secondary to gastrointestinal loss

Hypokalemia secondary to gastrointestinal loss:

1. Laxative abuse
2. severe or chronic diarrhea
3. Villous adenoma
4. congenital chloride losing diarrhea

Hypokalemia secondary to Renal loss:

1. Hypertension. alkaline urine, metabolic alkalosis:

1. Primary hyperaldosteronism
2. Liquorice ingestion
3. Excessive diuretic therapy
4. Excessive mineralocorticoid therapy for Addison's disease

2. Normotension , alkaline urine, metabolic alkalosis

Hyperplasia of the juxta glomerular apparatus with hyperaldosteronism

3. Alkaline Urine, metabolic acidosis:

Renal Tubular acidosis

1. Primary
2. Secondary

4. Acidic Urine , Metabolic acidosis:

Chronic ammonium chloride ingestion

Recovery phase of diabetic ketoacidosis

Recovery phase of acute tubular necrosis

5. **Antibiotic Therapy:**

Amphotericin B

Gentamycin

Carbenicillin

Ticarcillin

others

Pharmacological agents

1. Beta Agonists
2. Insulin
3. Barium
4. Epinephrine and norepinephrine
5. Glucocorticoids
6. Thiazide

TABLE-I

THE CHANNELOPATHIES

Channel affected	Sodium	Sodium	Calcium	Potassium
Disease	Hyperkalemic Periodic Paralysis	Paramyotonia Congenita	Hypokalemic Periodic Paralysis	Anderson disease
Inheritence	Dominant	Dominant	Dominant	Dominant
Gene	SCN4A	SCN4A	DHP receptor	KCNJ2
Channel Protein	Alphasubunit	Alpha subunit	Dihydropuridine receptor	Inward rectifying K' Channel
Myotonia (electrical)	+/-	++	-	-
Myotonia (Clinical)	+/-	-	-	-
Paramyotonia (Clinical)	+/-	+++	-	-
Episodic Paralysis	+++	+/-	+++	+
Onset	First decade	Paramyotonia at Birth	Latechildhood to third decade	childhood
Precipitating factors Increases with exercise	-	+++	-	+
Appears after exercise	++	-	++	-
Fasting	+	-	-	-
Carbohydrate load	-	-	+	-
Potassium load	++	+/-	-	-

THE CHANNELOPATHIES

Cold	+	+++	+	-
Pregnancy	++	-	+	?
Warm-up phenomenon	+	-	+	-
involvement of cranial muscles	+	++	-	++
muscle hypertrophy	-	-	-	-
permanent myopathy	++	-	++	+
Serum ck during attack	Increased	Increased 5 to 10 times	Normal to Slightly increased	Normal
Serum K during attack	Increased	Normal	Decreased	High, low or normal
Serum K between attacks	Normal	Normal	Normal	Normal
Significant myopathy	++	-	++	Tubular aggregates
Treatment	during attack glucose and calcium for prevention – acetazolamide CHO, Low K diet	Mexiletine if needed for myotonia	KCL during and acetazolamide between attacks	acetazolamide

K - Potassium
CHO - carbohydrate
+ mild
++ moderate
+++ severe

PATHOPHYSIOLOGICAL MECHANISM

The pathophysiology of hypokalemic periodic paralysis is not clear. Electrophysiologic studies performed in vitro on muscle fibers from hypokalemic patients revealed alterations in membrane excitability. These observations suggested that ion channels might be implicated in the pathophysiology of the disease.

Given the electrophysiologic data, the first strategy chosen was to test for linkage to known ion channel genes. The initial linkage studies were conducted with three families of Portuguese, German and French descent Positive iod scores were observed for markers localised on chromosome 1q31-32 establishing the hypokalemic periodic paralysis 1 locus. The calcium channel[1] α_1 subunit CACNLIA3 also called dihydropyridine receptor (DHP receptor) was mapped to the same 5 – c M interval as the hypokalemic periodic paralysis 1 locus. Three mutations were subsequently found in the coding sequence of CACNLIA3, establishing it as the hypokalemic periodic paralysis gene .

One mutation replaces a positively charged arginine by a weakly positive histidine in position 528 in segment S4 of domain II. The other two replace an arginine with either a histidine or a glycine in position 1239 segment S4 of domain IV . The ARG 528 His and Arg 1239 His mutations were present in

approximately 90% of the hypokalemic periodic paralysis families, each of them found in approximately 50% of cases. The phenotype was identical in terms of attacks and of development of a vacuolar myopathy. Incomplete penetrance was observed only with the ARG 528 HIS mutation. Characterization of the haplotypes segregating with the mutations demonstrated that the predominance of these two mutations was due not to a founder effect but to recurrence mutations.

Till date 7 mutations have been described in α_1 subunit of CACNLIA3 thus accounting for approximately 55-70% of all hypokalemic periodic paralysis.

These includes

ARG1239HIS

ARG528 HIS

ARG528GLY

ARG1239GLY

ARG1086CYS

ARG1086HIS

Other mutations involve sodium – channel[2] voltage gated, type IV α subunit. The gene has been mapped to chromosome 17q23.1-q25.3. This account for approximately 8 – 10% of hypokalemic periodic paralysis type II

Five mutations described to date that includes

ARG669HIS

ARG672HIS

ARG672GLY

ARG672SER

PRO1158SER

Some evidence exits that patients with this sodium channel mutation are phenotypically different form the more common CACNAIS form. These types of mutation are associated by the presence of myalgias following paralytic attacks; tubular aggregates instead of vacuoles in the muscle biopsy and worsening of symptoms by acetazolamide (sternbery et al. 2001)

CLINICAL FEATURES

Hypokalemic periodic paralysis is inherited as an autosomal dominant[7] disorder in 2/3rd of cases and sporadic in 1/3rd

- Males are most commonly affected with male to female ratio of 3 or 4:1)
- Females have a low penetrance
- Attacks characterically begin in adolescence
- Onset after 30 years is rare

- Attack frequency varies from days to years.
- Duration of single attack lasts from hours if mild to days it severe
- The frequency of attack tend to lessen with advancing age
- Typical attack comes on during the second half of the night or the early morning hours after a day of unusually strenuous exercise or a meal rich in carbohydrates.

Hypokalemic periodic paralysis is characterized by two forms :

1. Paralytic form
2. Myopathic form:

PARALYTIC FORM:

The weakness may be proceeded by certain prodromes such as excessive hunger, thirst, dry mouth, palpitations, sweating, diarrhea, vomiting and a sense of weariness or fatigue. Usually the patient awakens to discover a mild or severe weakness of the limbs. However diurnal attacks also occur, especially after a nap following a large meal. The attack evolves over minutes to several hours, at its peak it may render the patient so helpless as to be unable to call for assistance.

The distribution of paralysis varies. Limbs are affected earlier and often more severely than truncal muscle and proximal muscles are possibly more susceptible than distal ones. The legs are often weakened before the arms but exceptionally the order is reversed. The muscle most likely to escape are those

of eyes, face, tongue, pharynx, larynx, diaphragm, and sphincters, but on occasion even these may be involved. when the attack is at its peak tendon reflexes are reduced or abolished and cutaneous reflexes may also disappear. Sensation is preserved. As the attack subsides strength generally returns first to the muscle that were last to be affected.

Headche, exhaustion. diuresis and occasionally diarrhea may follow the attack. Myotonia is not seen: indeed clinical or EMG evidence of myotonia essentially excludes the diagnosis of hypokalemic Periodic paralysis. Rarely, death may occur from respiratory paralysis or derangement of the conducting system of the heart.

The atypical forms of presentation include:

1. Weakness of one limb or certain group of muscle
2. Bibrachial palsy
3. Transient weakness during accustomed activities.

MYOPATHIC FORM:

This form develops in approximately 25% of affected individuals and results in a progressive fixed muscle weakness that begins at extremely variable ages as exercise intolerance predominantly in the lower limbs. It occurs independent of paralytic symptoms and may be the sole manifestations of hypokalemic periodic paralysis.

Recognized trigger for hypokalemic periodic paralysis[18]

1. High carbohydrate diet
2. Large meals
3. salt
4. Sleep after unaccustomed exercise.
5. Medications eg: diuretics, insulin

The resting membrane potential of the skeletal muscle has been altered in these patients and when potassium level falls down the RMP goes to -50MV at which the muscles becomes inexcitable.

DIFFERENTIAL DIAGNOSIS:

The differentiation between different type of periodic paralysis are given in the table.

Periodic paralysis can be readily distinguished from

- **Guillian – Barre syndrome**

  Weakness is usually of the ascending type, antecedent infective episode might be present. Potassium levels may not be low. CSF analysis will be supportive.

- **Poliomyelitis**

  More asymmetrical, antecedent gastrointestinal manifestations might be present.

- **Cataplexy:**

  Which lasts only for few seconds or minutes and is precipitated by emotion.

- **Sleep Paralysis.**

  The episodes are very brief

- **Myasthenia gravis**

  Ocular involvement more common

- **Hysterical Paralysis.**

DIAGNOSIS:

Established by demonstration of low or low normal serum potassium during a typical paralytic attack and by excluding secondary causes of hypokalemia.

An important limitation is that the use of serum potassium to give a reliable index of true mild hypokalemia is associated with inaccuracies in the measurement of serum potassium. Potassium may be unintentionally released from the intracellular compartments during the collection of venous blood samples, released from platelets, as the blood coagulates prior to centrifugation of the sample or due to mild hemolysis.

These factors can elevate serum potassium by .5 mmol/l or more

Also, true potassium deficiency can be masked by acidosis, renal failure, or tissue destruction and liberation of potassium.

Electrocardiogram during attacks may show features characteristic of hypokalemia[27]

These includes

1. Flattening or inversion of 'T' waves
2. Prominence of 'U' waves
3. ST segment depression
4. Wide QRS complexes
5. Prolonged QT interval
6. Prolonged PR interval
7. Atrial and ventricular extrasystole.

Electromyogram:

The muscular weakness in this disease is associated with decrease in the amplitude, and eventual loss, of muscle action potentials and there is failure of excitation even by supramaximal stimulation of peripheral nerve or by strong voluntary effort. A decline in strength precedes loss of motor unit potentials and the failure of propagation of action potentials over the surface of fiber. The polarization potentials of muscle fibers measured by intracellular recordings are initially normal despite the failure of impulse propagation by the sarcolemma. One would expect the muscle fiber to be hyperpolarized as K moves into it ,

but it actually becomes depolarized. Rudel and associates attribute the latter change to an increased Na conductance.

Histopathological alteration in hypokalemic periodic paralysis[9]

The histopathological hallmark of the syndrome is a vacuolar myopathy, (Goldflam 1895). This can be seen in either primary or secondary periodic paralysis, but more often in the former than in the later. The vacuolation is more consistently associated with the permanent myopathy which develops after repeated attacks than with acute paralysis (Klein et al 1960, Mc Ardle 1963 Samaha 1965, Resnick & Engel 1967). The vacuoles are typically centrally located in the muscle fibers and usually one vacuole but at times several appear in a fiber in a single plane of sectioning. Some vacuoles are limited by a delicate membrane. Some are loculated, and some contain finely granular material staining positively for glycogen.

Electron microscopic studies have shown that the vacuoles arise as a result of proliferation and degeneration of membranous organelles within the sacrcoplasmic reticulum and transverse tubules.

Malignant hyperthermia (MH)[5]

It has been proven to allelic to hypokalemic periodic paralysis. All hypokalemic periodic paralysis patients must be considered at greatly increased risk to this life threatening complication of surgery. A persistently elevated CK Could be a hint to Malignant hyperthermia predisposition

PROVOCATIVE TESTING IN PATIENTS WITH SUSPICION OR HAVING SUSPECTTED PERIODIC PARALYSIS.

INITIAL THERAPY:

This test follows an overnight fast, Oral glucose 1-5 gm/kg is given over three minutes, (maximum of 100 gms)

Monitoring

(with patient at rest)

- Free flowing arterialized blood to be obtained baseline, every 30 mins upto 3 hours for potassium, sodium, chloride, co_2 glucose, then every 60 minutes for 5 hours.
- Strength of the muscle to be assessed at 30 minutes interval in 4 to 6 muscles based on muscle group involved during an attack.
- ECG to be checked every 30 minutes or continuous monitoring is used if available.

Comment

The nadir in serum potassium after oral glucose usually coincides with or followed by the peak rise in serum glucose. Potassium levels in normally after

oral glucose loading typically do not fall below 3.5 mmol /L . If weakness occurs, then treat as hypokalemic periodic paralysis.

If no weakness or adverse effects and if no medical contraindication following the initial test, intravenous glucose with insulin can be given.

Following an overnight fast, infuse intravenously a glucose load of 3 gms/d (max 200 gm) in water at a continuous rate over 1 hour. A bolus → IV insulin is given (.1unit/kg) 30 minutes after initiation of glucose infusion.

Monitoring (with patient at rest)

- Free flowing arterialized blood to be obtained baseline, every 30 mins upto 3 hours for potassium, sodium, chloride, co_2 glucose, then every 60 minutes for 5 hours.
- Strength of the muscle to be assessed at 30 minutes interval in 4 to 6 muscles based on muscle group involved during an attack.
- ECG to be checked every 15 minutes or continuous monitoring is used if available.

Caution: Intravenous loading tests should not be done in patients with significant renal, cardiac or hepatic disease or in diabetics. It should be done after admission in hospital.

Specialized provocative hormone infusion tests include

- Euglycemic insulin infusion over two hours started initially at insulin dose of 20mu/m2/min
- Intrabrachial arterial infusion of epinephrine

Comment:

These tests have the advantage of producing a more reproducible controlled fall in circulating potassium for either the whole body (euglycemic insulin infusion) or for the forearm tissues (eg: intra brachial epinephrine infusion.

BICYCLE TESTING FOR PERIODIC PARALYSIS[10]

Bicycle Ergometry Testing- 30 minutes test

1. Patient is tested in early afternoon or late morning. Breakfast is allowed but no strenuous exercise before the test. Each patient lies supine for 15-30 minutes with monitoring of baseline ECG and indwelling intravenous catherter is placed, for collection of free flowing samples.

   Exercise load in men 100 watts

   For women 60 watts.

Blood samples 5,10 minutes before the test

3,6,10,20 and 30 minutes during the test

3 and 10 minutes after the test

Pedal speed 60 r.p.m. ECG is monitored through out the tests.

MOLECULAR GENETIC TESTING:

This identifies disease causing mutations in CACNAIS or SCN4A in 80% of individuals meeting clinical diagnostic criteria.

TREATMENT[7]

Acute paralysis improves following administration of potassium salts.

Oral Kcl 0.2-0.4 mmol/kg should be given to patients with severe weakness repeated at 30 to 60 mins interval depending on the response of ECG serum potassium and muscle strength.

When patient is not able to swallow or when there is vomiting intravenous therapy may be necessary.

Small repeated bolus therapy of KCL (.1mmol/kg) may be administered over 5-10 mins with careful monitoring of heart.

PREVENTION OF ATTACK:

Diet has not received the same attention in the treatment of hypokalemic periodic paralysis . Increased attention to diet is highly justified due to its potential for decreasing the frequency of paralytic attacks, the possibility of preventing or slowing permanent muscle weakness and reduced drug requirements in some individuals. Dietary fat may prove to be an essential key to dietary modulation of these disorders.

With all the negative emphasis on fat and cholesterol consumption often one forgets the fact that dietary fat is essential in maintaining health. One important characteristic of dietary fat that is often overlooked is its role in

slowing stomach emptying. Fat in a meal decreases the rate at which other food components are moved from the stomach to the small intestine thus decreasing the opportunity for a meal to dump its load of carbohydrates into the blood all at once.

Simple sugar and even carbohydrates with out the inhibition of fat are rapidly digested and absorbed. Carbohydrates are the primary stimulus for insulin secretion and the products of protein digestion also stimulate the release of insulin into the circulation.

Insulin balance is an important consideration in energy metabolism and in the dietary control of channelopathies like hypokalemic periodic paralysis. Carbohydrate loading is a well established trigger for paralytic attack in periodic paralysis and research has demonstrated a connection between ATP sensitive potassium channels in the pathogenesis of hypokalemic periodic paralysis.

The other dietary measures include low-sodium diet (160 meq/day) and avoidance of large meals.

The patient should also avoid exposure to cold as this also reduce the frequency of attacks.

Pharmacotherapy for prevention of attacks

- Prophylactic admistration of potassium salts 5 to 10gms of oral KCL in an unsweetened aqueous solution prevents attacks in many patients, and this can be maintained indefinitely
- Acetazolamide (125 – 1000 mg/day) usually abolishes attacks.
- In occasional patients attacks may be not respond to or may be worsened by acetazolamide.
- Dichlorphenamide 50 - 1000 mg per day may also be useful
- Spiranolactone 25-1000 mg/day may also prevent attacks
- Triameterene 25 -100 mg/day may be tried.

Acetazolamide can produce mild metabolic acidosis which perhaps influences the potassium shifts that occur in this disorder.

Side effects of Acetazolamide:

- Tingling in the digits
- Tendency for formation of renal stones
- Hypersensitivity reactions

For the late progressive polymyopathy. Dalakas and Engle report successful restoration of strength by the long term administration of the carbonic anhydrase inhibitor dichlorphenamide. Regular exercise (not too strenuous) to keep the patient fit is desirable.

GENETIC COUNSELLING:

Hypokalemic Periodic Paralysis is inherited as autosomal dominant disorder. Most individuals diagnosed with hypokalemic periodic paralysis have an affected parent. The Proportion of cases caused by a denova gene mutation is unknown. Offspring of a proband have a 50% risk of inheriting the mutation. Penetrance is about 90% in males and may be as low as 50% in females depending on the causative mutation. Prenatal testing is possible if the disease causing mutation has been identified in the Prohand, however, requests for prenatal testing for conditions such as hypokalemic periodic paralysis that don't affect the intellect and have some treatment is not advisable.

PRE OR POST OPERATIVE PARALYSIS

Because of the risk of paralysis preceding or following anesthesia precautions should be taken during administration of anesthesia to individuals with hypokalemic periodic paralysis. These patients should be considered as susceptible to malignant hyperthermia and managed with non – triggering anesthetic technique.

General guidelines for perioperative care include close control of plasma potassium concentration, avoidance of large glucose and salt loads carbohydrate poor diets, maintenance of body temperature and acid base

balance and careful use of neuromuscular blocking agents with continuous monitoring of neuromuscular function (Hofer et al 2001)

TESTING OF RELATIVES AT RISK:

When a disease causing mutation is identified in a proband, molecular genetic testing of at risk asymptomatic family members is appropriate because of the risk of un-expected acute paralysis and / or malignant hyperthermia.

When the results of presymptomatic testing are not known, the at risk family members must be considered at risk for complications and precautions must be taken, particular in the administration of anesthesia and avoidance of risk factors.

AIM OF THE STUDY

To evaluate cases of hypokalemic periodic paralysis with reference to the clinical presentation, mode of diagnosis, various methods of treatment and outcome of the different modalities of therapy. To find out the ways of preventing acute attacks, early diagnosis of attacks and when they occur to treat them effectively. To analyse the age incidence and also gender prevalence.

THE STUDY

The study is conducted to evaluate the cases of hypokalemic periodic paralysis with reference to the clinical presentation, laboratory parameters, treatment and outcome.

Settings

This study is conducted in the tertiary care centre, Government general Hospital, Chennai , Medical wards.

Type of study

Prospective

No of cases

40

Period of study

From July 2004 to July 2006

METHODS AND MATERIALS

Cases admitted in the medical wards with history of flaccid weakness of limbs with low serum potassium or electrocardiographic changes suggestive of hypokalemia were included in this study.

Also cases referred from other hospitals for evaluation of hypokalemic paralysis to find out secondary causes of hypokalemia.

After admission, a thorough clinical examination of the patient was done after eliciting detailed history and blood was sent for biochemical analysis such as blood urea, sugar, serum creatinine, serum electrolytes including sodium and potassium.

Electrocardiogram was taken simultaneously. Treatment was initiated soon after admission.

INCLUSION CRITERIA

Existence of one of the following:

1. Observation of the paralytic attack by a physician or history typical of paralytic attack. Hypokalemia during the attack was often observed but not a prerequisite.
2. Progressive muscle weakness plus first degree relatives with hypokalemic periodic paralysis.
3. Characteristic histological findings in muscle biopsy.

EXCLUSION CRITERIA

1. Patient with history of systemic disorders eg: Diabetes mellitus, chronic kidney disease etc.
2. Patients with history of vomiting, diarrhea.
3. Patients on drugs such as steroids, insulin, diuretics, salbutamol, laxative etc,
4. Abnormal thyroid function test.
5. Abnormal arterial blood gas analysis.

PARAMETERS CONSIDERED FOR ANALYSIS WERE

1. Age
2. Sex
3. Past history of similar episode / episodes
4. Family history of similar episodes
5. Precipitating factor if any.
6. Serum potassium level on admission
7. Electrocardiographic changes
8. Treatment
9. Outcome

CLINICAL PROFILE OF HYPOKALEMIC PERIODIC PARALYSIS

Name Age Sex IP No.

DOA DOD.

CLINICAL CONTRIBUTORS

Mode of onset of weakness:

whether paraplegia or quadriplegia :

Ascending / Descending paralysis:

Time of onset of weakness:

Symmetric involvement :

Associated cranial nerve involvement:

Sensory system involvement:

Symptoms of autonomic system involvement :

Respiratory muscle dysfunction :

Precipitating factors:

Prodromal symptoms:

History of diarrhea , vomiting:

History of drug intake:

History of Diabetes, kidney disease:

History of thyroid disease:

Past history of similar episodes:

Number of episodes:

onset of first episodes:

Family history of similar episode:

CLINICAL EXAMINATION:

Whether Paraparesis / plegia:

Quadriparesis / plegia:

Cranial nerve involvement:

Involvement of neck muscle:

Reflexes :

Single breath count:

Evidence of myotonia :

LAB DATA

HB%

TC

DC

ESR

Renal function test.

Blood sugar

Urea

Sr. creatinine

electrolytes

ABG

Urine analysis – Sodium

Potassium

ECG in all leads

CXR PA view

Echocardiogram

USG - Abdomen

Thyroid function test

Serum CPK

THERAPEUTIC CONTRIBUTORS:

Pottasium supplementation

- Oral
- Intravenous
- Others

Recovery time.

Mortality

FINDINGS

AGE FREQUENCY

AGE	FREQUENCY	PERCENTAGE
≤ 20Yrs	8	20%
21 - 30Yrs	25	62.5%
31-40 Yrs	7	17.5%
TOTAL	40	100%

Around 60% cases were in their 3rd decades 20% of cases were in their 2nd decade

GENDER FREQUENCY

GENDER	FREQUENCY	PERCENTAGE
MALE	30	75%
FEMALE	10	25%
TOTAL	40	100%

Ratio :

M : F

3 : 1

PAST HISTORY	FREQUENCY	PERCENTAGE
Nil	24	60%
1 time	8	20%
2 times	4	10%
3 times	2	5%
4times	2	5%
TOTAL	40	100%

About 40% of the cases were found to have suffered similar attacks in the past.

FAMILY HISTORY

FAMILY HISTORY	FREQUENCY	PERCENTAGE
Present	15	37.5%
Absent	25	62.5%
TOTAL	40	100%

About 37.5% of the total number of patients had
first degree relatives with similar problem.

PRECIPITATING FACTOR

	FREQUENCY	PERCENTAGE
Carbohydrate diet+Sleep	8	20
Sleep	-	-
Exercise	-	-
Exercise+Sleep	2	5
Nil	30	75
TOTAL	40	100%

Good carbohydrate diet followed by sleep was found to be the culprit in many patients.

CLINICAL FEATURES	FREQUENCY	PERCENTAGE
Quadriparesis / Plegia	32	80%
Paraparesis /plegia	8	20%
TOTAL	40	100%

About 80% of the patients had presented with Quadriparesis / plegia

POTASSIUM LEVEL IN SERUM meq/L	FREQUENCY	PERCENTAGE
1.2	4	10%
2.1-3.0	22	55%
3.1-3.5	9	22.5%
3.6-4.0	4	10%
>4	1	2.5%
TOTAL	40	100%

Maximum number of patients had serum potassium levels between 2-3 meq/L

ECG	FREQUENCY	PERCENTAGE
Normal	8	20%
Abnormal	32	80%
TOTAL	40	100%

8 Patients had normal ECG despite of weakness.

TREATMENT	FREQUENCY	PERCENTAGE
Oral KCL alone	32	80%
Oral +IV Pot chlor	6	15%
Oral KCL + acetazolamide	2	5%
TOTAL	40	100%

Even though different modalities of treatment used almost 80% of patients had been treated with Oral potassium chloride alone.

RELEVANCE OF CLINICAL MANIFESTATIONS WITH POTASSIUM VALUES

CLINICAL	SERUM POTASSIUM IN meq/L					TOTAL
	1.2	2.1to 3.0	3.1 to 3.5	3.6to 4.0	>4	
Quadriparesis	3 7.5%	17 42.5%	9 22.5%	2 5%	1 2.5%	32 80%
Paraparesis	1 2.5%	5 12.5%	-	2 5%	-	8% 20%
TOTAL	4 10%	22 55%	9 22.5%	4 10%	1 2.5%	40 100%

RELEVANCE OF POTASSIUM VALUES AND ECG.

ECG	SERUM POTASSIUM IN meq/L					TOTAL
	1.2	2.1to 3.0	3.1 to 3.5	3.6to 4.0	>4	
Normal	1 2.5%	4 10%	-	2 5%	1 2.5%	8 20%
Abnormal	3 7.5%	18 45%	9 22.5%	2 5%	-	32 80%
TOTAL	4 10%	22 55%	9 22.5%	4 10%	1 2.5%	40 100%

AGE BY GENDER

AGE IN YEARS	MALE	FEMALE	TOTAL
≤ 20Yrs	6 15%	2 5%	8 20%
21 - 30Yrs	19 47.5%	6 15%	25 62.5%
31-40 Yrs	5 12.5%	2 5%	7 17.5%
TOTAL	30 75%	10 25%	40 100%

TREATMENT BY POTASSIUM LEVELS

TREATMENT	SERUM POTASSIUM IN meq/L					TOTAL
	1-2	2.1to 3.0	3.1 to 3.5	3.6to 4.0	>4	
Oral KCL alone	-	18 45%	9 22.5%	4 10%	1 2.5%	32 80%
Oral KCL+ IV KCL	4 2.5%	2 12.5%	-	-	-	6 15%
Oral KCL+acetazolamide	-	2 5%	-	-	-	2 5%
TOTAL	4 10%	22 55%	9 22.5%	4 10%	1 2.5%	40 100%

DISCUSSION

The age at which hypokalemic periodic paralysis presents is usually in the second decade[18] as per literature. But in this study, the commonest age group is in the third decade. The next is presentation in their second decade and less commonly in the Fourth decade . The disorder is less common after Fourth decade. In this study no one has presented with features of hypokalemic periodic paralysis after fourth decade, even though cases have been reported in their seventh decade also as evidenced by a cases report[19] published by Decaux O, Poinsingnon Y, Rosenbaum D, Sternberg B, Douissiere Jardel J, Jardel H.

This variation may be due to the fact that children less than 14 years are referred to Institute of Child Health, Chennai and also the Frequency of attacks decreases as the age advances, and also most of these patients have past history of similar episodes which they have ignored or treated elsewhere. This may limit analysis of the age adjusted data with literatures. So assessing the past history of a similar weakness is very important.

The male gender is commonly affected than females for every female patient approximately three males were affected. This can be attributed to the fact that the penetrance[8] is supposed to be mild in females as this is supported by study by Kawamura S , Ikeda Y, Tomita K. Watanabe N, Sekik .

Another important factor is that females might have a very mild disease and hence many times the manifestations are not obvious.

Most of the patients have first degree relative with a similar episodes. In my study around 40% of the patients have family history[21] of similar episodes. In a study conducted by Desilva HJ, Senanayake N around 40% of patients had family history of hypokalemic periodic paralysis.

As mentioned earlier, these patients can have repeated episodes of flaccid weakness. In between attacks, the patient will be absolutely normal. Even though the exact factors which determine the frequency of attacks are not known there can be certain factors which can precipitate acute attacks in particular patients.

The precipitating factors which have commonly been observed are a heavy carbohydrate diet followed good sleep. The less common presentation has been that the patient after a strenuous day and a heavy dinner goes to bed. on waking up early morning he finds that he is unable to move either his lower limbs or both upper and lower limbs . Hence these patients should avoid heavy meals and rather should take frequent small meals. Though it is reported in literature, no patient had weakness during or immediately following exercise, in our study group.

With regards to clinical presentation many of these patient had presented with flaccid quadriparesis / plegia. Some of the patient had presented with

flaccid paraplegia/paresis . Most of the patient had depressed tendon reflexes and plantar that was not elicitable. No patient had presented with sensory symptoms bladder or bowel involvement.

The duration of illness varied with each patient but most patients had recovery time that is between 12 and 24 hours. Only two patients had flaccid weakness that lasted for 48 hours.

Most of the patients had weakness of neck muscles. But none of the patients had difficulty in swallowing, breathing. Also none of the patient had cranial nerve involvement.

The diagnosis of hypokalemic periodic paralysis is supported by a low potassium level during the time of the attacks. Out of 40 patients about 85% of the patient had low serum potassium levels. It is observed that patients have suffered attack of paresis even in low normal range of serum potassium.

In our case study most of the cases had serum potassium level between 2 to 3 meq / L and some of the patients had levels between 1 to 2 meq /L .

Electrocardiographic changes[26] of hypokalemic periodic paralysis were seen in 80% of the patients. The common findings were disappearance of T waves and prominent U waves. Some of the patient had depressed ST segment. In 20% of patients, electrocardiogram were normal despite of low serum potassium level. Hence one should keep in mind that the ECG does not always correlate with serum potassium level.

In my study there is no correlation between the severity of the attack and the level of serum potassium. Also, there is no correlation between the duration of weakness and the initial serum potassium levels.

None of the patient had previous history of surgery. As there patient are at increased risk of developing malignant hyperthermia[5], a life threatening complication of anesthesia, the attending surgeon and anesthetist should be informed about this in case of surgery. Also the patients were counseled regarding this.

Some of the other investigations that would be useful are.

1. EMG
2. Muscle biopsy.

As per the study various treatment modalities have been used by different physicians. No single protocol has been followed. The most frequently used mode of treatment has been oral potassium chloride or a combination of acetazolamide with potassium chloride.

Six patients has been treated with Intravenous potassium chloride. All patients are instructed to take plenty of orange juices and tender coconut which is supposed to contain 70 meq /L of potassium.

Universally the outcome of any type of presentation has been good. But it has taken different time period for complete recovery. This would be due to three factors.

1. Absence of any particular protocol for treatment to be followed.
2. The potassium level at the time of presentation
3. The genetic variations.

But it is important to correct the hypokalemia at the earliest or other wise the patient can develop.

1. cardiac arrhythmias
2. Respiratory paralysis
3. Muscle fiber can suffer damage leading ultimately to progressive muscle weakness.

CONCLUSION

ON HYPOKALEMIC PERIODIC PARALYSIS

- Incidence ratio M: F = 3:1
- Commonest age group is in the third decade
- 40% have had similar attack in the past
- Flaccid quadriparesis was the commonest mode of presentation.
- About 37% of the patient had first degree relative with similar attacks
- Most of the patient have had serum potassium level between 2 to 3 meq/L
- ECG abnormalities has been observed in 80% of the patients most of these patients were treated with oral potassium chloride alone
- Outcome was good in all patients.

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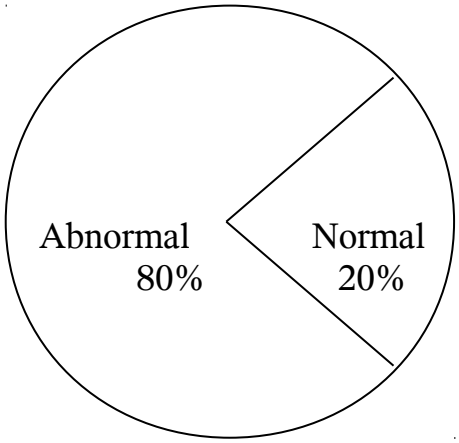
INCIDENCE OF ECG ABNORMALITIES IN HYPOKALEMIC PERIODIC PARALYSIS



AGE RELATED INCIDEME OF HYPOKALEMIC PERIODIC PARALYSIS

[

MASTER CHART

S.No	Name	I P. No	Age	Sex	Past* History	Family** History	Pre.*** Factor	Clinical presentation		Serum potassium level	ECG	Teatment		Outcome
								quadriparesis	parapare sis			Oral Kcl	Others	
1	Vedagiri	819635	33	M	-	-	-	-	+	3.6	-	+	-	Recovery
2	Karunakaran	815974	30	M	-	-	-	-	+	2.4	-	+	-	Recovery
3	Jettappan	815236	25	M	+	+	-	+	-	2.2	+	+		Recovery
4	Madhu	788087	16	M	-	+	+	+	-	2.0	+	+	IV KCL	Recovery
5	Panchacharam	819938	35	M	+	-	-	+	+	2.2	+	+	+Diamox	Recovery
6	Sridhar	812298	25	M	-	-	-	+	-	2.9	-	+		Recovery
7	Thiruvenkatam	829340	14	M	-	+	+	+	+	2.7	+	+		Recovery
8	Alavudeen	812032	21	M	-	-	+	+	+	3.8	+	+		Recovery
9	Sakthivel	815595	30	M	+	-	+	+	-	2.0	+	+	IV KCL	Recovery
10	Shankar	81627	18	M	+	-	-	+	-	2.6	+	+		Recover

S.No	Name	I P. No	Age	Sex	Past* History	Family** History	Pre.*** Factor	Clinical presentation		Serum potassium level	ECG	Teatment		Outcome
								quadriparesis	parapare sis			Oral Kcl	Others	
		5												y
11	Natarajan	787512	28	M	+	+	-	+	-	3.4	+	+		Recovery
12	Ramachandran	752197	20	M	-	-	-	+	-	2.8	+	+		Recovery
13	Srinivasan	753634	24	M	-	-	+	+	-	2.3	+	+	IV KCL	Recovery
14	Duraisamy	789618	35	M	+	+	-	+	-	2.4	+	+		Recovery
15	Vadivelu	814373	36	M	+	-	-	-	+	2.4	+	+		Recovery
16	Jeyamani	822544	20	M	+	+	-	+	-	2.1	+	+		Recovery
17	Mugundan	815268	24	M	-	-	-	+	-	3.5	+	+		Recovery
18	Manikandan	762048	27	M	-	+	+	+	-	2.5	+	+		Recovery
19	Iyanaar	834035	30	M	+	-	-	+	-	2.3	+	+	+Diamox	Recovery

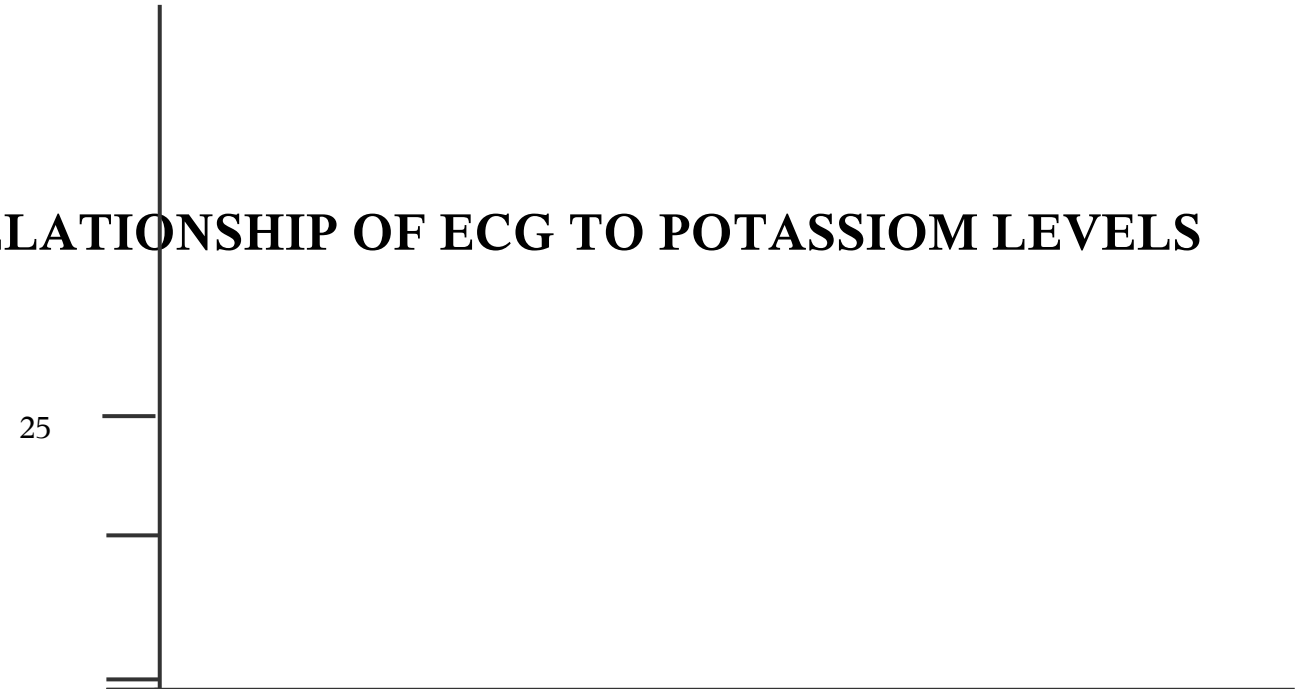
S.No	Name	I P. No	Age	Sex	Past* History	Family** History	Pre.*** Factor	Clinical presentation		Serum potassium level	ECG	Teatment		Outcome
								quadriparesis	parapare sis			Oral Kcl	Others	
20	Kanagaraj	823846	35	M	-	+	-	+	-	3.1	+	+		Recovery
21	Salaman	804923	29	M	-	-	-	+	-	3.4	+	+		Recovery
22	Vinayagam	839643	27	M	-	-	-	-	+	1.9	+	+		Recovery
23	Murugan	834650	21	M	-	+	+	+	-	2.7	-	+		Recovery
24	Srinivasalu	743385	30	M	+	-	-	+	-	2.2	+	+		Recovery
25	Gurusamy	745257	30	M	+	+	-	+	-	2.4	+	+		Recovery
26	Ahmed	775772	22	M	-	-	-	+	-	3.6	-	+		Recovery
27	David	775772	20	M	-	+	-	+	-	3.5	+	+		Recovery
28	Dhanasekar	781946	25	M	--	+	-	+	-	4.1	+	+		Recovery
29	Murugan	817593	28	M	-	-	-	+	-	3.9	-	+		Recovery

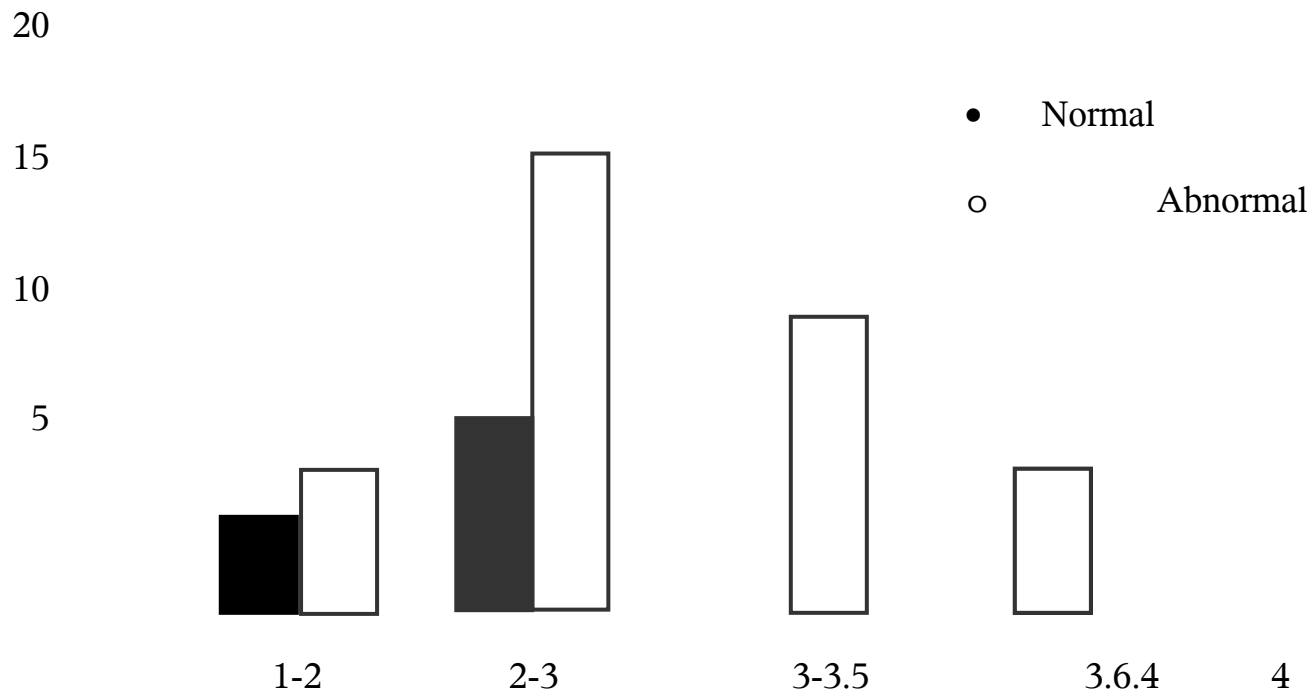
S.No	Name	I P. No	Age	Sex	Past* History	Family** History	Pre.*** Factor	Clinical presentation		Serum potassium level	ECG	Teatment		Outcome
								quadriparesis	parapare sis			Oral Kcl	Others	
30	Subramani	830976	30	M	-	+	-	+	-	3.2	+	+		Recovery
31	Ditshed	816940	28	F	+	-	-	+	-	2.3	+	+		Recovery
32	Vijaya	825887	37	F	+	-	+	+	-	2.7	+	+		Recovery
33	Sudarkodi	818136	22	F	+	-	-	+	-	2.2	+	+	IV KCL	Recovery
34	Jeyanthi	773383	28	F	-	+	-	+	-	3.4	+	+		Recovery
35	Bakiya	823229	36	F	+	-	-	-	+	2.3	+	+		Recovery
36	Umamaheswari	836591	29	F	-	-	+	-	-	3.3	+	+		Recovery
37	Maheswari	795388	20	F	-	+	+	+	-	2.7	-	+		Recovery
38	Kalaivani	729139	20	F	-	-	-	+	-	1.8	+	+	IV KCL	Recovery
39	Lakshmi	738852	22	F	-	-	-	+	-	3.1	+	+		Recovery

S.No	Name	I P. No	Age	Sex	Past* History	Family** History	Pre.*** Factor	Clinical presentation		Serum potassium level	ECG	Teatment		Outcome
								quadriparesis	parapare sis			Oral Kcl	Others	
40	Muniammal	838034	30	F	+	-	-	-	+	2.9	+	+		Recovery

- = Absent
+ = Present
* = Past History of similar episodes
** = Family History of similar epidodes
*** = Precipitating factor
ECG = Electrocardiogram
KCL = Potassium chloride
IV = Intravenous

RELATIONSHIP OF ECG TO POTASSIOM LEVELS




20
15
10
5
Normal
Abnormal
1-2
2-3
3-3.5
3.6.4
4